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(54) Test plate assembly defining discrete regions on a microporous membrane with low boundary distortion

(57) A biochemical test plate assembly for use in multiple simultaneous contact tests arranged in a fixed array of discrete regions on a single microporous membrane sheet provides less distortion of the boundaries of these regions than do pre-existing assemblies. The assembly contains two apertured plates 11, 13; an apertured gasket sheet 17 and a microporous membrane 19, both placed between the apertured plates; and a third plate 15 for placement beneath the apertured plates, having a recess which serves as a reservoir for liquids passing through the membrane. The improvement resides in the enclosure of the lower apertured plate by the upper apertured plate and a recess in the base plate, thereby sealing the lower apertured plate and the microporous membrane off entirely from the atmosphere. This eliminates evaporation of moisture from the edges of the membrane, and any lateral diffusion of biochemical species which might occur as a result due to capillary attraction. The floor of the base plate may slope towards a vacuum port 46.

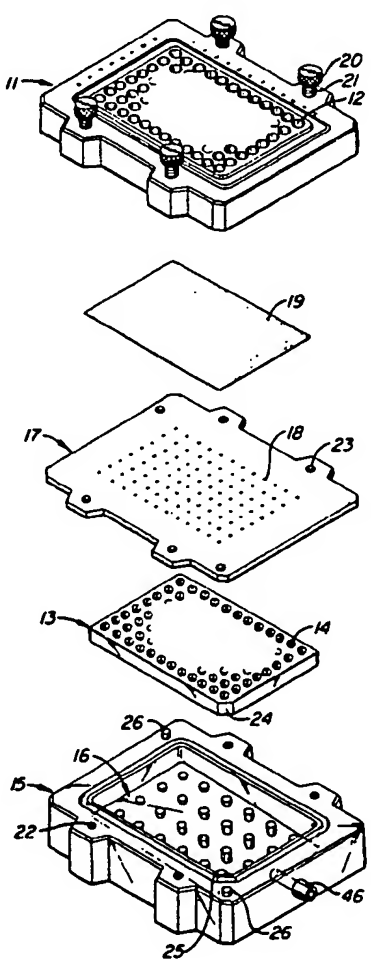

FIG. 1.

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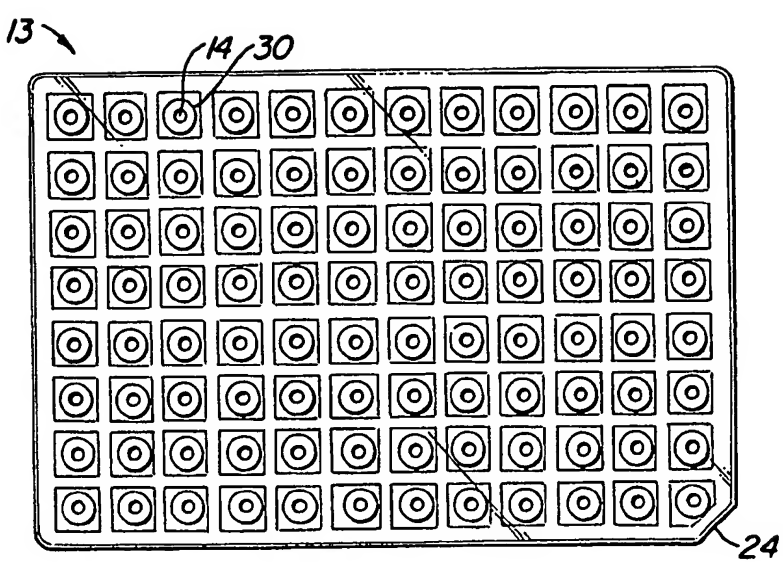

FIG._2A.

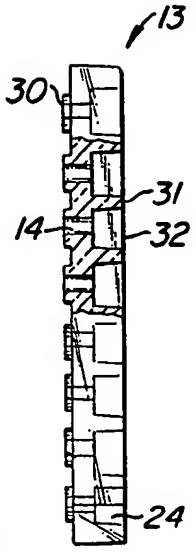

FIG._2B.

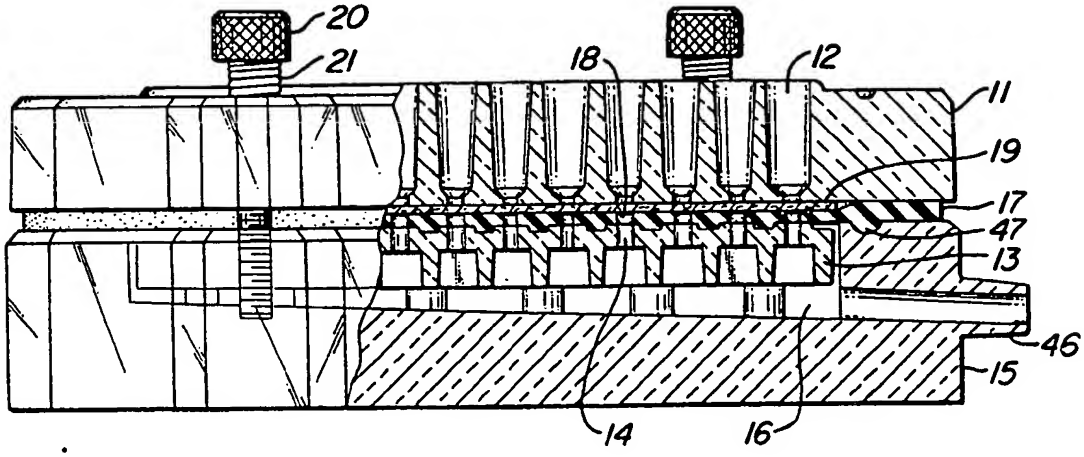

FIG._4.

SPECIFICATION

Test plate assembly defining discrete regions on a microporous membrane with a low boundary distortion

BACKGROUND OF THE INVENTION

This invention relates to an apparatus for biochemical testing and screening procedures involving the use of a microporous membrane.

A biochemical test plate assembly capable of handling multiple simultaneous tests involving a single microporous membrane is disclosed in Fernwood et al., U.S. Patent No. 4,493,815, Bio-Rad Laboratories, Inc., January 15, 1985. The assembly provides a standard 8-by-12 rectangular array of cylindrical wells, with the bottom of each well sealed by a common microporous membrane. The membrane in turn rests above a recess forming an enclosed chamber from which a vacuum may be drawn or which may be completely sealed against air loss thereby providing a static air cushion beneath the membrane. The device may thus be used for either (a) drawing a fluid containing biochemical species through the microporous membrane, or (b) supporting a static fluid above the membrane for an indefinite length of time. The exposed membrane regions collectively provide. an array of discrete test regions with highly defined boundaries. Accurate automated detections can then be performed on the membrane after it is removed from the assembly.

The assembly generally consists of two apertured plates (an upper and a lower) and a base plate containing a recess to form the vacuum chamber beneath the wells. The microporous membrane and an apertured gasket are placed between the two apertured plates. The membrane is thus the only obstacle between the upper plate apertures and the vacuum chamber, thereby permitting both flow-through and static contact procedures, depending on the air pressure in the chamber. The wells and flow passages are sealed from the surrounding room atmosphere by the apertured gasket between the two apertured plates, and a further gasket between the lower apertured plate and base plate.

It is critical that these seals be perfectly airtight so that prolonged tests can be done without loss of chamber pressure. This requires highly polished finishes at the surfaces where the seals are made, which adds considerably to the cost of manufacturing.

Furthermore, since the membrane must be fully moistened before assembly of the parts, the exposure of its outer edges to the atmosphere during the test procedures raises another disadvantage — evaporation from these edges. This induces outward migration of the biochemical species which have contacted the membrane through the outermost wells. The result is distortion of the outermost test regions on the membrane. This is a serious failing, since the lack of uniform contact areas obscures the test results in a number of ways.

SUMMARY OF THE INVENTION

An improvement over the device described above is offered by the present invention, in which the lower of the two apertured plates is fully enclosed by the remaining two plates. This reduces the number of seals which have atmospheric contact to a single seal between the two enclosing plates. The microporous membrane is thus sealed off from the atmosphere entirely, and evaporation from the membrane itself is eliminated as well as any lateral diffusion driven by the resulting capillary attraction. With these features, the assembly of the present invention overcomes both of the problems mentioned above, while still retaining the same versatility of use and function. The result is a test plate assembly which provides even greater accuracy and reproducibility.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is an expanded view of one embodiment of a test plate assembly according to the present invention;

FIG. 2A and FIG. 2B are a plan view and end view with cutaway, respectively, of the lower apertured plate shown as one of the components in FIG. 1;

FIG. 3A and FIG. 3B are a plan view and a side sectional view, respectively, of the bottom plate shown in FIG. 1; and

FIG. 4 is a side view in partial cutaway of the assembled parts of the embodiment shown in FIG. 1.

DETAILED DESCRIPTION OF THE DRAWINGS AND PREFERRED EMBODIMENTS

As in Fernwood et al., referenced above, the test plate assembly of the present invention is intended to accommodate a multitude of simultaneous biochemical tests, each in one of a series of discrete wells or reservoirs arranged in a horizontal array. Although the number, size and spacing of the wells may vary, the most common and versatile arrangement is one comprising 96 circular wells in an 8-by-12 rectangular array, with a center-to-center spacing of approximately 9mm, an arrangement used by a large variety of associated laboratory equipment. Other examples include oval or slotshaped wells with associated apertures of appropriate shape. For convenience, the drawings and the remainder of the description herein refer to a standard 96-well array.

FIG. 1 illustrates one embodiment of the test plate assembly of the invention. The assembly is designated by the numeral 10, its primary parts consisting of an upper plate 11 having a plurality of apertures 12 arranged in the aforementioned array; a middle plate 13,

are generally cylindrical, the diameter of each undergoing a reduction from the upper surface of the plate to the lower surface. This is useful in concentrating the biochemical species as it passes through the well and is deposited on the microporous membrane, improving the ease of detection and subsequent processing steps. To maximize the well capacity, the tapering portion is located toward the bottom of the aperture, providing a well capacity ranging from about 100 to about 1,000 microliters in volume.

As another feature, the apertures 18 in the sheet gasket 17 are of slightly smaller diameter than both those of the upper plate (at the narrower end) and the lower plate. In this way, the defined test area on the microporous membrane 19 is slightly smaller than the diameter of the apertures in the plates, and slight misalignments of either the plates or the gasket sheet will not affect the size of the test area, since it will still be in full contact with the liquid either held in or passing through the wells.

The plates may be constructed of any rigid inert material, preferably transparent so that the test fluids may be observed. Conventional materials will suffice, notably acrylic, polycarbonate, polypropylene or polysulfone. A convenient means of forming the plates is by injection molding. Since this avoids the need for machining of the plates individually, open spaces or gaps are easily incorporated into the structures to reduce the weight and the amount of plastic required. The embodiments shown in the drawings are simplified, however, for a better understanding of the functional aspects of the construction.

As in the structure disclosed in Fernwood et al., referenced above, the test plate assembly of the present invention may be used for two basic modes of operation --- forcibly drawing a fluid through the membrane, and retaining a fluid above the membrane for a prolonged period of time. The former may be achieved by drawing a vacuum through the vacuum port 46, while the latter is achieved by sealing the port 46 from the atmosphere and retaining a slight positive pressure in the recess of the base plate below the middle plate. These functions may be performed either individually or sequentially in a wide variety of biochemical laboratory procedures, with improved results in terms of accuracy, reproducibility, and lack of distortion.

The foregoing description is offered primarily for purposes of illustration. Although a variety of embodiments has been disclosed, it is not intended that the present invention be limited to the particular structures or methods of operation set forth above. It will be readily apparent to those skilled in the art that numerous modifications and variations not mentioned here can still be made without parting from the spirit and scope of the invention as claimed hereinbelow.

CLAIMS

1. A biochemical test plate assembly for use in both filter assays and static blot assays, said assembly comprising:

an upper plate having a plurality of apertures;

a middle plate having a plurality of apertures aligned with the apertures of said upper plate;

a lower plate having a recess which, when said lower plate is covered by said upper plate, defines an enclosed chamber of sufficient size to contain said middle plate;

means for forming an air-tight peripheral seal between said upper plate and said lower plate around said enclosed chamber;

a microporous film of sufficient size to span the apertures of said upper plate when placed between said upper plate and said middle plate, yet lie within the area defined by said peripheral seal; and

a gasket sheet having a plurality of apertures aligned with the apertures of said upper plate and adapted to form a lateral seal around the adjoining edges of each aligned pair of apertures when compressed between said upper plate and said middle plate.

2. A biochemical test plate assembly according to claim 1 further comprising means for applying a vacuum to said enclosed chamber.

3. A biochemical test plate assembly according to claim 1 in which said recess includes a floor and means for supporting said middle plate above said floor, thereby defining a space between said middle plate and said floor to receive liquid passing through the apertures in said middle plate.

4. A biochemical test plate assembly according to claim 3 further comprising a vacuum port communicating said space with the exterior of said lower plate, and wherein said floor slopes toward said vacuum port.

5. A biochemical test plate assembly according to claim 3 in which said supporting means is comprised of a plurality of posts extending up from said floor.

6. A biochemical test plate assembly according to claim 1 further comprising means for securing said upper plate, said microporous film, said gasket sheet, said middle plate and said lower plate together to compress said gasket sheet and said peripheral seal forming means sufficiently to form said lateral seals and said peripheral seals, respectively.

7. A biochemical test plate assembly according to claim 1 in which said peripheral seal forming means is comprised of a compressible gasket.

8. A biochemical test plate assembly according to claim 1 in which said peripheral seal is a compressible gasket, and the range of compression of said peripheral seal exceeds that of each said lateral sheet around the ad-